

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Gordon S. Sacks

Aimee B. Sacks

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For: ORAL DELIVERY FORMULATIONS OF
L-GLUTAMINE

Group Art Unit: 1609

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CERTIFICATE OF ELECTRONIC TRANSMISSION
37 C.F.R. § 1.8

I hereby certify that this declaration is being electronically
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August 13, 2007

Date

Steve L. Highlander

DECLARATION OF GORDON SACKS UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

I, Gordon Sacks, do declare that:

1. I am the Gordon S. Sacks that is named as an inventor on the above-captioned application. I hold the position of clinical associate professor in the School of Pharmacy at the University of Wisconsin. I am a citizen of the United States residing at N3892 Highway TT, Columbus, WI.

2. In the development of the present invention, we first combined only L-glutamine with frozen water in a popsicle mold. The result was a precipitation (or clumping) of L-glutamine in the bottom of each popsicle. When the popsicles were removed from the mold, this precipitation was visually obvious as a white clump at the uppermost tip of the popsicle (i.e., representing the bottom of the popsicle when inverted in the mold). As a result, a number of different mediums were tested in an attempt to “suspend” the L-glutamine and prevent precipitation. We finally found that pudding would provide the necessary the appropriate medium to suspend the L-glutamine and provide a uniform dispersion throughout.

3. Our first attempt to create a popsicle formulation comprised only of 5 g of L-glutamine mixed in sterile water was performed as follows. The method involved the use of a 30-mL syringe to pull up 25 mL of sterile water and squirted into a large glass beaker (500 mL). One level scoop of L-glutamine (5 g) was added to the beaker and mixed into the water until the mixture did not have any visible clumps. A ¼ teaspoonful of Orange Kool-Aid® was added for flavoring (per 25 mL sterile water and 1 scoop of L-glutamine). A 10 cc syringe was used to pull up an additional 5 mL of sterile water and squirted into a 500-mL beaker to assist with dissolving the Kool-Aid®. The mixture was poured into one popsicle slot (this amount will fill one popsicle mold slot—therefore may use 60 mL and 2 scoops of L-glutamine to fill 2 popsicles slots at a time). Each entire mold contains 10 slots to make a total of 10 popsicles in a batch. The entire mold was placed in a freezer (15°F) for overnight. The entire popsicle mold was removed from the freezer the next morning and warm water was run over the bottom of the mold for 5 minutes. The metal lid was removed from the mold. Individual popsicles were removed by gently moving the popsicle stick back and forth while pulling back on the stick at the same time. When

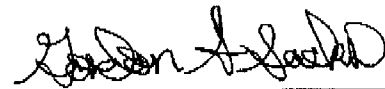
individual popsicles were removed, it was obvious that the L-glutamine had precipitated to the bottom of the mold (now representing the top of the popsicle). The top of each popsicle had a “white” tip with the remaining portion appearing orange due to the flavoring. This is considered to represent an unstable formulation. Upon placing the popsicle in the mouth, it was immediately obvious that the formulation was unpalatable. For comparison, some “placebo” popsicles were manufactured at the same time. A “placebo” popsicle was tasted and found to be quite palatable. To confirm the content of the precipitant, both L-glutamine and placebo popsicles were shipped on dry ice for analysis by Scientific Research Consortium, Inc., St. Paul, MN, 55113. The L-glutamine popsicles contained on average 20145 $\mu\text{mol/L}$ of glutamine or 1734 mg of glutamine per gram of sample. High concentrations of L-glutamic acid (average 1732 $\mu\text{mol/L}$ or 0.3279 mg per gram of sample) were also observed, reflecting a breakdown or instability in L-glutamine. In comparison, the “placebo” popsicles contained 10.2 $\mu\text{mol/L}$ of glutamine or 0.015 mg of glutamine per gram of sample (L-glutamine is present in small quantities of foodstuffs, *i.e.*, pudding, so this accounts for the presence of L-glutamine in the placebo popsicles). Levels of glutamic acid were not detected in the “placebo” popsicles.

4. Next, a formulation of 5 g of L-glutamine mixed in Hunts Vanilla Pudding was prepared as follows. The method involved the use of a 30-mL syringe to pull up 25 mL of pudding and squirted into large glass beaker (500 mL). A 10-mL syringe was used to pull up 5 cc of sterile water and squirted into a 500-mL beaker with the pudding. One level scoop of L-glutamine (5 g) was added to the beaker and mixed into water and pudding until the mixture appeared smooth without any visible clumps. A $\frac{1}{4}$ teaspoonful of Orange Kool-Aid® was added for flavoring (per 25 mL pudding, 5 mL water, and 1 scoop of L-glutamine). The mixture was

poured into a popsicle slot in the mold (this amount will fill one popsicle slot - therefore 50 mL pudding, 10 mL water, and 2 scoops of Glutamine can be used to fill 2 popsicle slots at a time). The entire mold was comprised of 10 popsicle slots. The entire mold was placed in a freezer (15°F) for overnight. The popsicle mold was removed from the freezer the next morning and warm water was run over the bottom of the mold for 5 minutes. The metal lid was removed from the mold. Individual popsicles were removed by gently moving the popsicle stick back and forth while pulling back on the stick at the same time. When individual popsicles were individually observed, there was no apparent precipitant and the entire popsicle appeared orange equally throughout. Both L-glutamine and placebo popsicles from this new batch were sent for analysis by Scientific Research Consortium. The L-glutamine popsicles contained on average 144.6 $\mu\text{mol/L}$ of L-glutamine or 116.9 mg of glutamine per gram of sample. The “placebo” popsicle concentrations were similar to the previous batch, containing 9.7 $\mu\text{mol/L}$ of L-glutamine or 0.014 mg of glutamine per gram of sample. Glutamic acid was not detected in “placebo” nor L-glutamine containing popsicles.

5. I declare that all statements made herein of my own knowledge are true, and that all statements of my own belief are believed to be true, and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code.

8/13/07
Date


Dr. Gordon S. Sacks